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## GUEST EDITORIAL

# Dry Eye Disease

**D**ry eye symptoms, reported by about 25% of patients, are one of the most common reasons for patient visits to eye-care professionals.<sup>1</sup> As various ocular surface conditions or diseases can lead to the same ocular symptoms, diagnosing, treating, and managing patients with dry eye symptoms can be challenging and frustrating to both clinicians and patients. Since the notable Tear Film and Ocular Surface Society's international workshops on Dry Eye Workshop and meibomian gland dysfunction (MGD),<sup>2,3</sup> awareness of how significantly dry eye symptoms negatively impact quality of life has risen. In the past decade, clinicians and scientists have made significant strides in improving care for patients with dry eye symptoms. This special issue of *Optometry and Vision Science* highlights a collection of reviews, original articles, clinical reports, and clinical perspectives that provide readers with updates regarding the diagnosis, treatment, and management of dry eye symptoms that result from various causes. Our contributor articles are reported here under the topics of Risk Factors, Diagnosis, Treatment and Management, and Clinical Perspectives.

### Risk Factors

Prevalence of dry eye varies considerably depending on diagnostic criteria, study designs, and regions of the world where studies are conducted. It has been reported that among women, Asians are significantly more likely to experience severe dryness symptoms.<sup>4</sup> Several known risk factors of dry eye are applicable to Chinese patients, and some distinctive dietary factors may be protective in this population.<sup>5</sup> Of known risk factors, contact lens wear is highly associated with dry eye symptoms; however, mechanisms responsible for this association are not clearly understood. Contact lens wear may be associated with meibomian gland atrophy; however, conflicting results have been reported and a longitudinal prospective study is warranted.<sup>6</sup> Contact lens-induced dry eye and binocular vision disorders are reported to share several common symptoms.<sup>7</sup> Further understanding about the relationship between these disorders can help clinicians to better manage contact lens-induced dry eye.

Another common risk factor for dry eye symptoms is topical antiglaucoma ophthalmic medications and their associated preservatives. We learn that increasing the frequency of antiglaucoma medication doses or types of drops increases the odds of having ocular surface disease and dry eye symptoms.<sup>8,9</sup> Some nonpreserved glaucoma medications may also have adverse effects on ocular surface health, resulting in a higher prevalence of ocular surface diseases among treated glaucoma patients.<sup>8</sup> Laser-assisted *in situ* keratomileusis (LASIK) is another significant risk factor; it injures the subbasal nerve plexus during the lamellar cut of the procedure. Nearly 50% of post-LASIK patients experience dry eye symptoms.<sup>10</sup> Blink

anomalies can significantly exacerbate post-LASIK dry eye symptoms.<sup>11</sup> Some cases of post-LASIK dry eye are neuropathic in etiology and warrant treatment of the underlying neuralgia rather than treatment of aqueous-deficient or evaporative dry eye, according to our authors.<sup>10</sup>

One of the most common types of evaporative dry eye is thought to be MGD. Meibomian glands are the main source of tear lipids, which are essential for retardation of tear aqueous evaporation. We learn that patients with a history of acne treatment using isotretinoin can also have dry eye symptoms because of damaged meibomian glands.<sup>12</sup> The effect of isotretinoin on the meibomian glands likely mimics its effects on the sebaceous glands of the skin in the treatment of acne.<sup>12</sup> Consequently, it is important for clinicians to be aware of isotretinoin-associated MGD, especially on young adults. It is also important to note that another common cause of evaporative dry eye, frequently underdiagnosed, is lagophthalmos or incomplete blink.<sup>13</sup>

### Diagnosis

A stable tear film is essential for maintaining ocular surface homeostasis and for providing good vision and ocular comfort. Understanding mechanisms responsible for tear film stability may be facilitated with the aid of infrared thermography described here.<sup>14</sup> Ocular surface cooling always precedes tear film breakup.<sup>14</sup> The lag time between tear cooling and breakup is explained by the time necessary to first disrupt the tear lipid layer that eventually forms a localized rupture, which accelerates evaporation.<sup>14</sup> Tear film stability can be assessed with an invasive method (e.g., instilling fluorescein dye on the eye) or with a noninvasive method (e.g., placido rings projecting on the precorneal tear film or other custom-built optical devices). However, the invasiveness of fluorescein application can potentially perturb the tear lipid layer, causing an inaccurate assessment of tear film stability; therefore, the volume of fluorescein dye should be minimized. The traditionally accepted diagnostic threshold of dry eye using tear breakup time is 10 seconds. It is reported that using a traditional threshold of 10 seconds may yield false-positive cases if applied on Asian populations.<sup>15</sup> In another study, a direct comparison with automated and traditional measures of tear film breakup shows poor agreement, perhaps because each method exhibits poor repeatability.<sup>15,16</sup> Further research is needed to refine and improve methods for assessing tear film stability as it is considered an important end point in clinical trials.

Increased tear osmolarity can be amplified by either increased tear evaporation or decreased tear supply. An accurate measurement of tear osmolarity on a localized ocular surface is not a trivial task and is currently not possible. Taking osmolarity measurements from the

tear meniscus is the basis for current osmometers. The utility of these tools in a clinical setting continues to be debatable relative to their reflection of what truly happens to the precorneal tear film.<sup>16,17</sup> In addition to natural lability of tear film and instrument variability, we have a report of test outcomes of tear film being climate dependent.<sup>18</sup>

In recent years, *in vivo* laser scanning confocal microscopy, providing *in vivo* cytology of the ocular surface, has been reported as a useful tool to diagnose neuropathic dry eyes and monitor treatment effect by measuring density of corneal nerves and inflammatory cells, as inflammation plays an important role in the pathogenesis of many dry eye cases.<sup>19</sup>

## Treatment and Management

A number of our articles here address both treatment and management of dry eye. Understanding tear film constituents and regulatory mechanisms for natural production of tear components can be used to develop new concepts for potential treatment strategies. Mucins play a major role in maintaining ocular surface homeostasis by lubricating and protecting the ocular surface as well as providing immunomodulatory function, acting as antimicrobial factors and preventing pathogens from binding to the ocular surface and clearing away pathogens.<sup>20</sup> An ophthalmic solution containing diquafosol tetrasodium offers an alternate treatment option to restore ocular surface integrity by stimulating goblet-cell secretion of ocular mucins.<sup>21,22</sup> For advanced cases of aqueous tear deficiency or ocular surface diseases, other treatment and management options are available, such as thermal and electrocautery of the lacrimal puncta, lid surgeries such as tarsorrhaphy, amniotic membrane, or scleral lens fitting.<sup>23</sup>

In today's society, even healthy eyes can experience temporary discomfort because of prolonged reading or viewing of computers or other electronic devices. Our authors offer software programs available for computers or smartphones to remind users to take visual breaks or blink more frequently to minimize stress to the tear film.<sup>24</sup> Other authors, in a review, draw attention to the fact that there are conflicting reports about the benefits of Omega-3 supplements and raise questions that warrant a longitudinal randomized controlled clinical trial to provide appropriate guidance on formulation, dosage, and duration of this essential fatty acid.<sup>25</sup> Eyelid margin debridement has gained much attention in recent years and studies, including a report in this issue, noting improvements in symptoms and signs after the procedure for patients with Sjogren or non-Sjogren dry eye.<sup>26</sup> Self-applied heat therapy has been the mainstay of therapy for MGD; however, a clinical series reported here reveals that not all warm compresses are equally effective.<sup>27,28</sup> Although much more costly than traditional warm compresses, some symptomatic patients with MGD find LipiFlow (Thermal Pulsation System) treatment to be beneficial. One team of authors suggests that an appropriate patient selection may increase patient satisfaction with this procedure.<sup>29</sup>

## Clinical Perspectives

Experts from different parts of the world have varying opinions about the most viable diagnostic methodologies and treatments.<sup>13</sup> In fact, dry eye disease may be the wrong term to describe an eye

that is not desiccated. Arguments are made that an etiology-based diagnosis allows clinicians to more effectively treat and manage dry eye symptoms, compared with symptom-based or definition-based approaches.<sup>13,30</sup> Until more novel treatment strategies are developed to restore and/or enhance tear gland function and ocular surface integrity, many treatment options addressing the signs and symptoms will remain primarily palliative. But as noted in this issue, hope for advanced treatments emerging through the pipeline is on the horizon.

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